

Computational Studies on Carbohydrates: I. Density Functional *Ab Initio* Geometry Optimization on Maltose Conformations

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ABSTRACT: *Ab initio* geometry optimization was carried out on 10 selected conformations of maltose and two 2-methoxytetrahydropyran conformations using the density functional denoted B3LYP combined with two basis sets. The 6-31G* and 6-311++G** basis sets make up the B3LYP/6-31G* and B3LYP/6-311++G** procedures. Internal coordinates were fully relaxed, and structures were gradient optimized at both levels of theory. Ten conformations were studied at the B3LYP/6-31G* level, and five of these were continued with full gradient optimization at the B3LYP/6-311++G** level of theory. The details of the *ab initio* optimized geometries are presented here, with particular attention given to the positions of the atoms around the anomeric center and the effect of the particular anomer and hydrogen bonding pattern on the maltose ring structures and relative conformational energies. The size and complexity of the hydrogen-bonding network prevented a rigorous search of conformational space by *ab initio* calculations. However, using empirical force fields, low-energy conformers of maltose were found that were subsequently gradient optimized at the two *ab initio* levels of theory. Three classes of conformations were studied, as defined by the clockwise or counterclockwise direction of the hydroxyl groups, or a flipped conformer in which the ψ -dihedral is rotated by $\sim 180^\circ$. Different combinations of ω side-chain rotations gave energy differences of more than 6 kcal/mol above the lowest energy structure found. The lowest energy structures bear remarkably close resemblance to the neutron and X-ray diffraction crystal structures. © 2000 John Wiley & Sons, Inc. *J Comput Chem* 21: 1204–1219, 2000

Keywords: density functional; *ab initio*; carbohydrates; maltose; geometry optimization; conformational analysis

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Introduction

The computational study of large complex oligosaccharides requires an empirical force field designed to reproduce, as accurately as possible, carbohydrate conformational structural properties and energies. One would like to use *ab initio*-derived carbohydrate structures to critically observe conformationally dependent geometry changes, and to use these variations in geometry to improve currently available empirical force fields. This force-field development procedure was described previously¹ for amino acids, peptides, and small polypeptides. In the peptide examples, extensive molecular orbital calculations had established important conformationally dependent structural changes that were subsequently used in fitting empirical parameters to establish a refined peptide force field.² This methodology was successful in producing a useful force field for peptides and proteins, and should be a successful way to derive a refined force field for carbohydrates.³ Unfortunately, the quantity and level of *ab initio* molecular orbital data for disaccharides is much less than that available for peptides. The work presented here attempts to correct for the lack of high-quality theoretical molecular structure data for complex carbohydrates.

In this article, we present results of density functional *ab initio* molecular orbital calculations⁴ on the disaccharide maltose and the model compound, 2-methoxytetrahydropyran (2-MTHP). 2-MTHP is of interest because it is one of the smallest molecules to retain the glycosidic linkage that forms the structural basis of many different carbohydrates. The structural properties of conformers of 2-MTHP have previously been studied using *ab initio* methods, in particular at the MP2/6-31G* level,⁵ and this work provides data that can be used to compare with our calculations. Further, the molecular parameters around the anomeric carbon and the effect of the anomeric differences on the ring conformations were not previously described in detail.⁵ These structural parameters and their variation with changing conformation are of particular interest to us in the development of an empirical force field for carbohydrates.

Computational Methodology

The introduction of density functional theory (DFT) into molecular system⁴ allowed the introduc-

tion of electron correlation in a more economical procedure relative to MP2 or MP4 methods. The DFT methods have afforded opportunities of performing structural analysis of moderately large carbohydrate molecules in a relatively short time. We use the B3LYP^{6,7} functional and two basis sets, denoted 6-31G* and 6-311++G**. The GDIIS method⁸ (direct inversion of the iterative subspace), and the eigenvector following (EF) algorithm^{9,10} were used to optimize the electronic wave functions and geometry, respectively. Optimization was considered satisfactory if energy differences between cycles of optimization were less than 1×10^{-6} Hartree and a gradient of less than 3×10^{-4} a.u. was achieved. At the termination of the gradient optimization, geometry changes between optimization cycles were generally less than one part in 10^5 , meaning that change in bond lengths between optimization cycles amounted to less than 10^{-4} Å, and less than 0.001° and 0.01° for associated bond and torsional angles, respectively. Both the B3LYP/6-31G* and B3LYP/6-311++G** calculations were carried out using the Parallel Quantum Solutions, Fayetteville, AR (PQS version 2.0) software and QS4-400S, QS4-500S, QS4-600S hardware. The eigenvalue following routine in the PQS software was found to be very efficient in convergence to an energy minimum for maltose. The InsightII graphics program (version 4.0.0P) from Molecular Simulations, Inc., San Diego, CA, was used for visualization and structure building purposes.

Calculations and Results

NOMENCLATURE

We use the following notations for the hydroxymethyl side-chain orientations: ($\omega 1$ and $\omega H1$) and ($\omega 1'$ and $\omega H1'$) refer to the O5—C5—C6—O6 and C5—C6—O6—HO6 dihedral angles (see Fig. 1). The prime refers to the reducing sugar residue. When numerical values are not used, the following shorthand form is useful.

Tt(g^- , g^+)	O6 <i>trans</i> to O5, the ring oxygen; and, t, HO6 <i>trans</i> to C5 (g^- , and g^+ also refer to the <i>gauche</i> orientation of the HO6 hydrogen atom)
G^-	C6—O6 bond <i>gauche</i> to both C5—O5 and C5—C4 bonds
G^+	C6—O6 bond <i>gauche</i> to both C5—O5 and C5—H bonds

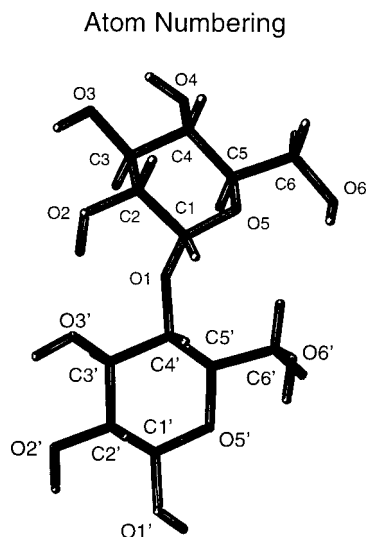


FIGURE 1. Atom numbering scheme for maltose conformations.

These dihedral angles are often described in the literature as tg, gg, and gt for only the rotation about the C5—C6 bond. In this article, they will appear as Tg^+ , G^-g^+ , etc. where the first letter refers to the C5—C6 bond and the second refers to the C6—O6 bond rotation. In the historical development of the nomenclature using small letters for just the C5—C6 rotation, one was not often concerned with the position of the hydroxyl hydrogen. In this work, we must carefully define the hydroxyl rotational states, and for this reason we have used the notation above. The hydroxyl groups will be described using standard χ^i notation.

2-Methoxytetrahydropyran

Experimental studies on 2-methoxytetrahydropyran have resulted in an enthalpy difference between the axial and equatorial anomers of 1.21 kcal/mol in the gas phase,¹¹ and this experimental energy is close to the energy differences found from these *ab initio* results reported in Table I. Two minimum energy configurations of 2-methoxytetrahydropyran were studied by B3LYP/6-31G* geometry optimization. Our interest was to establish in detail the geometry around the anomeric carbon, in particular the positions of the hydrogen atoms and anomeric carbon relative to the orientation of the lone-pair electrons on the two oxygen atoms. To that end we have chosen the two lowest energy conformations of the axial and equatorial forms to study.

A careful examination of Table I is very informative in that the structural changes around the anomeric carbon are quite large. The bond lengths are consistent with those found previously,⁵ with significant C1—O1 bond shortening in the equatorial anomer. What has not been pointed out previously are the conformationally dependent geometry changes in the C1—H1 bond length and O1—C1—H1 and C2—C1—H1 angles around the H1 hydrogen atom. A difference of 0.011 Å for a C1—H1 bond length between the axial and equatorial anomers and bond angle changes of $\sim 3.8^\circ$ between anomers are significant. We cannot stress enough the importance of correctly positioning the hydrogen atoms during the development of an empirical force field.

It is also of interest to examine the tetrahydropyran ring conformation. The major changes in the rings found between anomers are in the dihedral angles about the ether bonds. Going from the axial to equatorial anomer, the two dihedral angles, C3—C4—O5—C1 and C4—O5—C1—C, change from values less than $\pm 60^\circ$ to values a few degrees greater than $\pm 60^\circ$. The ϕ dihedral angles (see Table I) from the B3LYP/6-31G* calculations are larger in magnitude than the MP2/6-31G* values of 61.1° for axial and -62.5° for the equatorial anomer⁵ but the trend toward a larger value for the equatorial anomer is preserved. The B3LYP/6-31G* Cartesian coordinates for axial and equatorial 2-methoxytetrahydropyran are listed in Table II.

Maltose

β -Maltose is a disaccharide composed of an α - and a β -D-glucopyranose ring joined by an α -(1 \rightarrow 4)-glycosidic linkage. The anomeric carbon is substituted in the axial configuration, and the hydroxyl conformations are shown in Figure 2 for the 10 energy minimized maltose conformations reported here. The three-dimensional structure of a disaccharide is primarily determined by the conformation about the glycosidic linkage. However, the conformational behavior of the glycosidic linkage is controlled by a subtle balance of many different interactions arising from each ring and its functional groups as well as interactions between rings across the glycosidic bridge. The conformational preferences of the backbone and hydroxyl groups for maltose were first examined using a preliminary version of the AMB99C force field,¹²⁻¹⁴ and many minimum-energy conformations with dihedral ϕ and ψ angles from different regions of

TABLE I.
B3LYP/6-31G* Energies, Geometry, and Molecular Parameters of the Axial and Equatorial Forms of
2-Methoxytetrahydropyran.^a

	Axial Form	Equatorial Form	Difference (Axial – Equatorial)
Energy (Hartrees)	–386.299853	–386.297880	0.001973
(kcal/mol)	–242406.85	–242405.61	1.24
Bond lengths (Å)			
C—O1	1.420	1.421	–0.001
O1—C1	1.411	1.390	0.021
C1—O5	1.418	1.426	–0.008
C1—C2	1.530	1.525	0.005
C2—C3	1.536	1.537	–0.001
C3—C4	1.536	1.536	0.000
C4—C5	1.528	1.530	–0.002
C5—O5	1.434	1.424	0.010
H(C,t)—C	1.093	1.093	0.000
H(C,g ⁺)—C	1.101	1.101	0.000
H1—C1	1.100	1.111	–0.011
Bond angles (deg.)			
C—O1—C1	113.72	114.21	–0.85
O1—C1—O5	112.40	108.71	3.86
C1—O5—C5	113.92	112.46	–0.18
O5—C1—C2	112.07	110.87	1.36
C1—C2—C3	111.28	110.34	1.05
C2—C3—C4	109.77	110.54	–0.73
C3—C4—C5	110.02	110.03	–0.32
C4—C5—O5	111.78	111.20	0.58
H(C,t)—C—O1	106.76	106.51	0.37
H(C,g ⁺)—C—O1	111.11	111.10	0.02
H(C,g [–])—C—O1	111.82	111.57	0.08
H1—C1—O1	109.71	110.26	–0.59
H1—C1—O5	103.83	107.86	–4.27
H1—C1—C2	111.29	110.34	–0.01
Dihedral angles (deg.)			
C—O1—C1—O5 (ϕ)	63.75	–64.88	—
H(C,t)—C—O1—C1	178.27	–175.42	6.31
C1—C2—C3—C4	–51.83	–51.39	–0.44
C2—C3—C4—C5	52.97	51.01	1.96
C3—C4—C5—O5	–55.80	–55.55	–0.25
C4—C5—O5—C1	58.17	61.56	–3.39
C5—O5—C1—C2	–56.40	–61.59	5.19
O5—C1—C2—C3	53.11	55.86	–2.75

^a The total calculated B3LYP/6-31G* energy can be compared to MP2/6-31G*, Axial: –385.0438408 (Hartrees), and Equatorial: –385.0326716 (Hartrees).⁵ C1 is the anomeric carbon atom.

conformational space were chosen for study. Although by empirical calculations several conformations studied are not the lowest energy configurations of hydroxyl groups for that particular set of bridging dihedral angles, the use of multiple conformers of both backbone and side chains

allows examination of geometry arising from relatively small changes in the backbone dihedral angles.

The size and conformational complexity of maltose presents unique problems in geometry optimization. Although one would hope that the min-

TABLE II.
B3LYP/6-31G* Cartesian Coordinates for Axial and Equatorial 2-Methoxytetrahydropyran.

Atom		Axial Form ^a			Equatorial Form		
		x	y	z	x	y	z
1.	C5	−0.963133	−1.230604	0.311919	−1.175195	−1.225807	−0.244654
2.	H	−1.688410	−1.836662	0.862926	−1.968121	−1.817537	0.222614
3.	H	−1.401089	−0.972013	−0.662697	−1.568896	−0.822928	−1.195244
4.	O5	−0.793347	−0.043159	1.097761	−0.898622	−0.159676	0.658006
5.	C1	0.131798	0.881383	0.550138	0.075244	0.747720	0.147169
6.	H1	0.179420	1.682631	1.302595	−0.314171	1.164049	−0.806700
7.	O1	−0.303768	1.411742	−0.683014	0.265940	1.765595	1.074155
8.	C	−1.494198	2.179184	−0.586160	−0.876596	2.584867	1.283757
9.	H	−1.361621	3.032047	0.097626	−1.700444	2.010684	1.732476
10.	H	−1.708513	2.556445	−1.589193	−0.566170	3.382654	1.962706
11.	H	−2.339564	1.577178	−0.232126	−1.223024	3.031393	0.338614
12.	C2	1.507188	0.251363	0.321549	1.406547	0.041049	−0.087022
13.	H	2.159625	0.987455	−0.160480	2.128613	0.754343	−0.500462
14.	H	1.933457	0.022281	1.306509	1.780542	−0.282722	0.891785
15.	C3	1.400045	−1.034207	−0.511408	1.214180	−1.166040	−1.019642
16.	H	2.377854	−1.526326	−0.577142	2.148815	−1.732254	−1.107010
17.	H	1.098197	−0.778718	−1.534725	0.968758	−0.810074	−2.031131
18.	C4	0.357895	−1.973103	0.113873	0.076816	−2.064837	−0.510494
19.	H	0.192060	−2.856160	−0.516749	−0.152135	−2.857219	−1.234753
20.	H	0.716105	−2.330757	1.088799	0.377919	−2.552260	0.425829

^a The largest atomic gradient for the axial form is −0.0000311 au on C5, and for the equatorial form, 0.0000421 au on C1.

imum energy conformation found by empirical calculations was also a minimum on the *ab initio* energy surface, it is not certain that this is the case for these complex systems even with a refined empirical force field. For example, previous empirical calculations report a global minimum energy position near $\phi = -45^\circ$ and $\psi = -35^\circ$. Several attempts to find a low-energy structure at this position using preliminary 3-21G HF followed by B3LYP/6-31G* were only partially successful, the energies of the minima found being ~ 2 kcal/mol higher in energy than the lowest energy conformations reported in Table III. Further, it is possible to generate a very low-energy conformation by empirical methods only to find a lower energy conformation that differs in one hydroxyl group rotation when optimized using the DFT/*ab initio* programs. The DFT/*ab initio* optimization methods will generally not climb over significant energy barriers and will often not find the lower energy conformer, but occasionally they will find a new conformation. For this reason we cannot say for certain that the DFT/*ab initio* global minimum energy conformation has been found, even though we believe that the preliminary empirical global minimum has been found through exhaustive searching. In Table III, we present struc-

tural parameters for 10 B3LYP/6-31G* and five B3LYP/6-311++G** geometry optimized β -maltose conformations. The full table (IIIS) of B3LYP/6-31G* molecular geometry parameters can be found in Supplementary Materials.

To our knowledge, there are no *ab initio* calculations on maltose of equivalent level with which to compare these structures, although some model alcohols and glucopyranose ring systems have been studied at the levels of theory used here.^{7, 15–17} Analysis of the results presented in Table III and Supplementary Material suggests that variations in the hydrogen bond linkages both about the rings and interring transmit subtle changes in hydrogen bond orientation around the molecule and result in changes in dihedral angles far from the original modified hydrogen bond. This long-range cooperativity clearly complicates the study of disaccharides. Although the conformations reported here are similar in many ways, we observe dihedral angle changes in the ring structures of several degrees, changes in bond angles at the bridging ether, anomeric, and exo-anomeric effects, and subtle but important changes in bond angles and bond lengths as a result of the complete molecule undergoing a

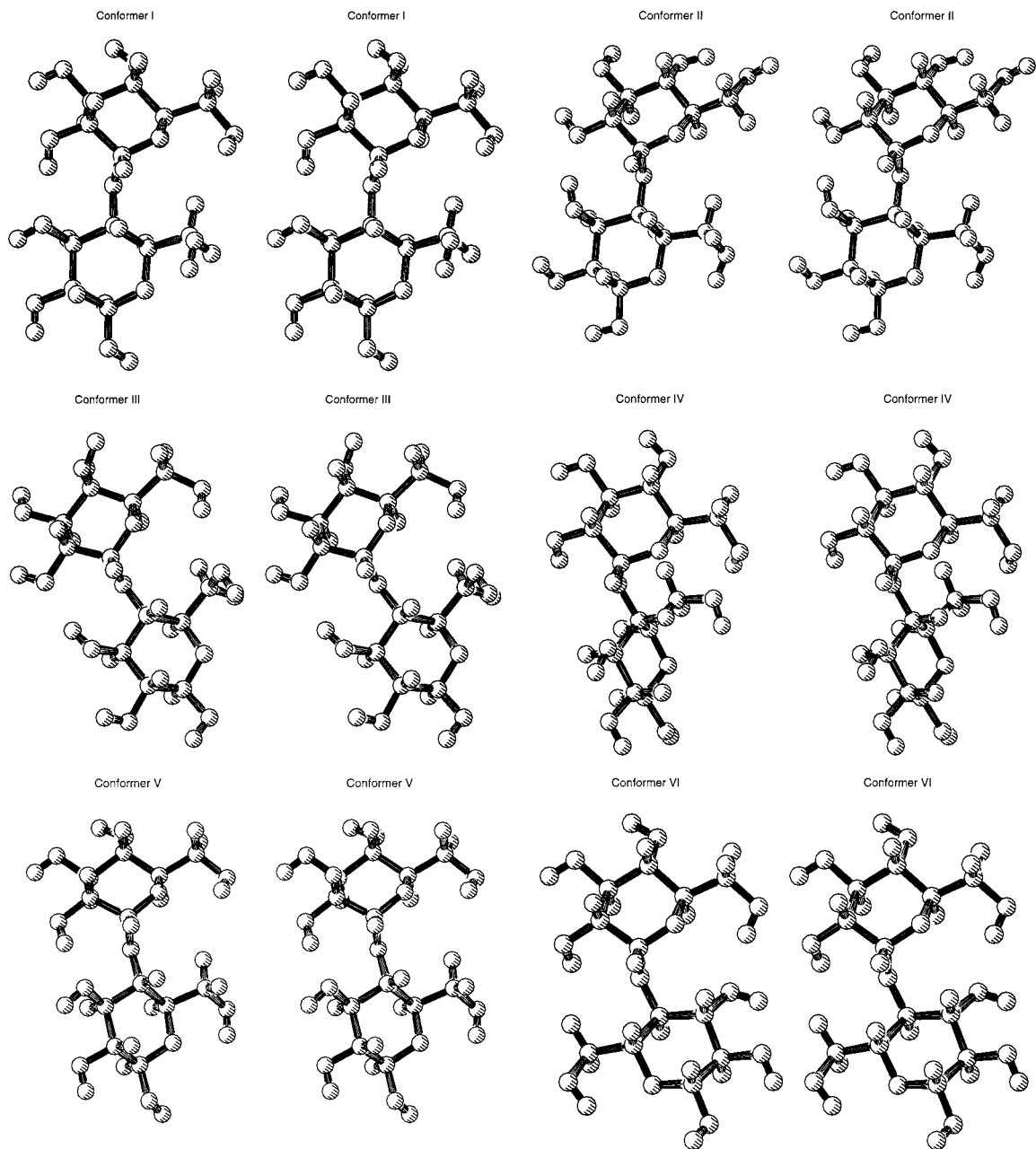


FIGURE 2. Stereo diagrams of Conformers I through X.

flexing process as the cooperativity of the hydrogen bonding pattern is changed.

Also of interest is the consistency achieved with the calculations reported in Table III and Table IIIS in the Supplemental Material. When a bond length or angle is not involved in a conformationally directed change, the geometry values are within several thousandths of an Ångström in bond length, and several tenths of a degree in bond angle. This consistency carries throughout all the calculations

reported herein, and allows isolation and examination in some detail of observed conformationally dependent geometry changes.

Comparing the calculated values around the axial glycosidic bond with the average structural parameters obtained experimentally from X-ray analysis give us a picture of the variances expected from conformationally dependent structural changes. For example, in Table IV we compare some standard experimental structural data from Tables 3.22 and 4.2

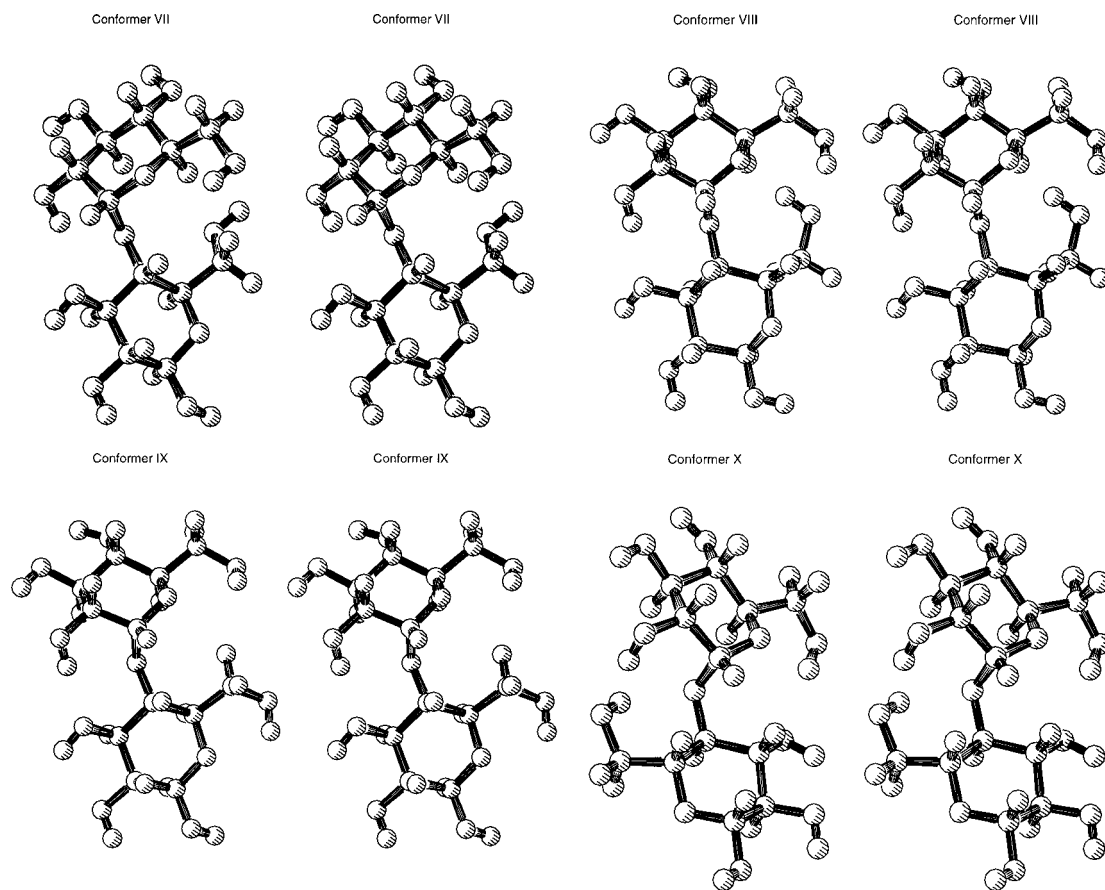


FIGURE 2. (Continued)

of Rao et al.,¹⁸ with a value calculated as an average of our B3LYP/6-31G* results. No attempt was made to convert calculated parameters to experimental units, i.e., r_e vs. r_g values.

The experimental and DFT/*ab initio* results are in excellent agreement, even though there are large conformationally dependent differences that do not show up in the calculated average values. Further, one must be aware that most of the calculated DFT/*ab initio* conformations have never been found in the crystallographic state, and so are not included in the experimental averages. We discuss the structural differences in a later section when each type of conformer is described.

Discussion

TYPE I CONFORMERS

Conformers I, IV, V, VII, and IX are considered to be of Type I, as all have counterclockwise pointing hydroxyl groups and only the two

6- and 6'-position hydroxymethyl groups differ in conformation. Conformer VIII also has counterclockwise pointing hydroxyl groups, but is treated as a separate type because of the complex hydrogen-bonding arrangement. Four different starting conformations moved upon optimization to the region of Conformer I space during DFT/*ab initio* gradient optimization. These are defined by their starting bridging dihedral angles: $\phi_H, \psi_H = -36^\circ, -29^\circ; -21^\circ, -16^\circ$; and two around $-31^\circ, -22^\circ$ that resulted in gradient converged structures of: $\phi_H, \psi_H = -9.2^\circ, 5.7^\circ; -9.7^\circ, 5.3^\circ; -9.3^\circ, 5.4^\circ$; and $-9.4^\circ, 5.5^\circ$, respectively. The largest energy difference between converged conformers was ~ 0.04 kcal/mol, confirming that energy and structural convergence had been achieved using the convergence criteria described previously. The starting structures (pregradient optimized) also differed in dihedral angles of the hydroxyl groups, the χ^2 group being $+4^\circ$ in one case, and -34° in another. The ω_1 and ω_1' dihedral angles were in the region of $+60^\circ$ and -60° , respectively, for all starting conformations. In the starting conformations of the four

TABLE III.
Energies and Geometry of Conformations of β -Maltose at the B3LYP/6-31G* and B3LYP/6-311++G**, in Parenthesis, Levels of Theory.^a

	I	II	III	IV	V
Energy (Hartrees)	-1297.89338 (-1298.34998)	-1297.88997 (-1298.34749)	-1297.89019 (-1298.34630)	-1297.88976 (-1298.34712)	-1297.88910
Energy Difference (kcal/mol)	0.00 (0.00)	2.14 (1.50)	2.00 (2.31)	2.27 (1.80)	2.68
Gradient	0.00008	0.00016	0.00010	0.00015	0.000015
Bond lengths (Å)					
C1—O1/C1'—O1'	1.422 (4)/1.395	1.408 (7)/1.396 (8)	1.406 (7)/1.396 (7)	1.439 (8)/1.394	1.418/1.394
C5—C6/C5'—C6'	1.524 (2)/1.526 (3)	1.526/1.526 (3)	1.522 (1)/1.526 (4)	1.525 (2)/1.525 (3)	1.522/1.528
HO6—O6/HO6'—O6'	0.968 (4)/0.976 (4)	0.968 (1)/0.973 (65)	0.975 (67)/0.971 (63)	0.975 (68)/0.972 (65)	0.971/0.971
HO2—O2/HO2'—O2'	0.979 (3)/0.971 (64)	0.973 (66)/0.973 (65)	0.972 (65)/0.972 (65)	0.973 (66)/0.971 (65)	0.979/0.971
Bond angles (deg.)					
C1—O1—C4'	119.15 (0.33)	117.37 (0.93)	115.62 (6.69)	114.81 (5.45)	117.49
O1—C1—O5/	111.68 (0.37)/	111.54 (6)/	111.81 (0.94)/	112.67 (5)/	111.16/
O1'—C1'—O5'	109.07 (8.85)	106.37 (5.91)	106.22 (5.77)	109.01 (8.78)	109.33
H1—C1—O5/	105.76 (0)/	105.31 (0.17)/	105.52 (0.30)/	105.68 (6.50)/	105.28/
H1'—C1'—O5'	109.10 (0.24)	109.25 (0.38)	108.96 (9.17)	108.88 (9.09)	109.44
HO2—O2—C2/	109.15/107.3	106.41/105.51	106.67/105.94	105.32/107.10	109.33/
HO2'—O2'—C2'	(110.34)/(108.39)	(107.59)/(107.36)	(107.89)/(107.40)	(106.71)/(107.37)	107.10
HO4—O4—C4	105.84 (107.21)	106.51 (107.81)	108.63 (9.79)	105.80 (7.15)	105.72
Dihedral angles (deg.)					
C4'—O—C1—O5 (ϕ)	107.99 (112.26)	109.42 (107.65)	99.40 (102.62)	64.18 (6.54)	108.12
C4'—O—C1—H1 (ϕ H)	-9.18 (-4.69)	-7.41 (-9.06)	-17.81 (-14.50)	-52.86 (-50.54)	-7.93
C1—O1—C4'—C—5' (ψ)	-114.44 (-109.96)	-147.76 (-140.47)	-135.75 (0.62)	-153.42 (2.83)	-143.17
C1—O1—C4'—H4' (ψ H)	5.74 (10.67)	-28.61 (-20.95)	-17.28 (-16.75)	-35.17 (-34.45)	-23.85
O6—C6—C5—O5/	55.65 (8.97)/	-178.17 (7.39)/	67.53 (6.83)/	61.03 (2.90)/	58.72/
O6'—C6'—C5'—O5'	-63.14 (2.03)	58.32 (60.48)	-69.16 (7.85)	-60.58 (2.42)	60.05
HO2—O2—C2—C3'/	90.60 (87.36)/	-41.57 (5.07)/	-47.77 (8.10)/	84.36 (5.05)/	149.53/
HO2'—O2'—C2'—C3'	-179.21 (6.74)	-48.59 (-51.58)	-49.87 (-52.11)	-176.10 (4.38)	-179.71

TABLE III.
(Continued)

	VI	VII	VIII	IX	X
Energy (Hartrees)	−1297.883150	−1297.884813	−1297.89307 (−1298.34749)	−1297.89057	−1297.88592
Energy Difference (kcal/mol)	6.42	5.38	0.19 (1.56)	1.77	4.68
Gradient	0.00010	0.00016	0.000075	0.00013	0.000065
Bond lengths (Å)					
C1—O1/C1'—O1'	1.423/1.393	1.423/1.395	1.412 (3)/1.394 (5)	1.421/1.394	1.427/1.393
C5—C6/C5'—C6'	1.521/1.528	1.521/1.531	1.528 (4)/1.541 (39)	1.523/1.528	1.520/1.539
HO6—O6/HO6'—O6'	0.975/0.972	0.971/0.970	0.975 (67)/0.979 (72)	0.971/0.971	0.974/0.973
HO2—O2/HO2'—O2'	0.973/0.971	0.974/0.971	0.980 (74)/0.971 (64)	0.980/0.971	0.981/0.971
Bond angles (deg.)					
C1—O1—C4'	119.11	115.82	120.13 (119.88)	119.41	118.92
O1—C1—O5/O1'—C1'—O5'	113.31/109.33	112.75/109.06	110.53 (0.42)/109.06 (0.32)	111.63/109.34	110.78/108.98
H1—C1—O5/H1'—C1'—O5'	105.05/109.32	105.58/109.19	105.90 (0.82)/109.33 (8.88)	105.86/109.25	106.24/109.36
HO2—O2—C2/HO2'—O2'—C2'	105.19/107.14	105.24/106.91	108.95 (10.13)/107.01 (8.35)	109.23/107.02	110.34/107.00
HO4—O4—C4	105.97	105.79	105.85 (7.23)	105.89	105.99
Dihedral angles (deg.)					
C4'—O—C1—O5 (φ)	83.44	73.68	110.35 (12.18)	108.17	94.75
C4'—O—C1—H1 (φH)	−34.16	−43.80	−6.50 (−4.44)	−9.02	−22.83
C1—O1—C4'—C5' (ψ)	72.28	−146.00	−104.63 (2.55)	−114.37	85.16
C1—O1—C4'—H4' (ψH)	−171.38	−27.40	17.38 (19.31)	7.05	−158.83
O6—C6—C5—O5'	71.58/	59.46/	86.39 (3.53)/	56.89/	67.60/
O6'—C6'—C5'—O5'	54.43	150.63	165.26 (2.71)	55.82	−177.93
HO2—O2—C2—C3/	73.49/	83.03/	84.32 (0.40)/	89.61/	78.04/
HO2'—O2'—C2'—C3'	−176.61	−178.54	179.53 (−177.86)	−179.11	−179.48

^a Missing geometry parameters (B3LYP/6-31G*) may be found in Table IIIS, supplementary material, or obtained as listings of coordinates from the authors.

TABLE IV. Comparison of Standard Pyranosides and B3LYP/6-31G* Calculated Molecular Dimensions for Maltose.

	Standard Exptl. (Ref. 24)	Ave. Calcd. Table III	Δ (Exptl. – Calcd.)
Bond lengths (Å)			
C—C (ring)	1.526	1.529	–0.003
C—C (exo)	1.516	1.525	–0.009
C—O (exo)	1.420	1.423	–0.003
Axial glycosidic bond. $\alpha(1 \rightarrow 4)$ linked disaccharides			
C5—O5	1.434	1.440	–0.006
C1—O5	1.419	1.409	0.010
C1—O1	1.415	1.419	–0.004
O1—C4'	1.435	1.429	0.006
Bond angles (deg)			
C—C—C (ring)	110.4	109.7	0.7
C—C—O (ring)	110.0	109.3	0.7
Axial glycosidic bond angles. $\alpha(1 \rightarrow 4)$ linked disaccharides			
C5—O5—C1	114.0	113.4	0.6
O5—C1—O1	112.1	111.9	0.2
C1—O1—C4'	116.7	117.7	–1.0
Ring torsion angles, axial			
C—C—C—C	53.0	54.0	–1.0
C—C—C—O	56.0	55.6	0.4
C—C—O—C	60.0	61.7	–1.7

convergent structures the hydroxyl groups were directed in the counterclockwise direction, while the ω -dihedral angles were directed clockwise.

Conformer I is nearly conformationally identical to the neutron diffraction/X-ray crystal molecular structures.^{19–23} In particular, the DFT/*ab initio* bridging dihedral angles (see Table III) are close to those ϕ_H – ψ_H values determined experimentally (4.8°, 13.3°, Gress¹⁹; 3.9°, 12.2°, Quigley²⁰; 5.6°, 15.9°, Chu²¹; –3.6°, 4.1°, Takusagawa²²; –7.6°, –15.8°, and –8.1°, –25.5°, Tanaka²³). It is only in subtle details that one finds differences between the calculated structure and the experimental structures, which may be a result of the crystal lattice packing effects. A comparison of the neutron diffraction molecular dimensions with Conformer I is presented in Table V in an attempt to isolate some differences in structure that could be attributed to crystal packing.

The agreement of the bonding structural parameters of Conformer I with experimentally derived molecular geometry is very close, making it difficult to attribute differences to crystal packing. If one can attribute anything to packing effects, it may be the angle of the twist between the reducing and nonreducing rings, where differences of

11° to 14° are found, the crystal packed structure being somewhat flatter overall than the calculated structure. The most obvious differences occur in the values of the dihedral angles of the hydroxyl groups where hydrogen-bonding interactions in the crystal between water molecules and maltose create directional forces that show up as large variance in dihedral angles. In the crystalline form of maltose, there are 10 intermolecular interactions with water molecules listed by French et al.,²⁴ so it is remarkable that the calculated and experimental conformations should be as similar as our calculations show. Differences between calculated and experimental bond lengths are close to precision limits even without correcting for thermal vibrational or other terms. Bond angles are within a few degrees, and even the dihedral angles of the ring structures are close. The small differences in backbone conformation (i.e., ϕ_H and ψ_H) between experimental and calculated values, clearly suggests that the vacuum DFT/*ab initio* structure is in the same global energy minimum as the experimental structure and that possibly, the backbone conformation in the crystal environment is not strongly dependent upon the hydrogen bonding network being either intra- or intermolecular.

TABLE V. Comparison of Several Molecular Parameters between Conformer I (Table III) from the B3LYP/6-31G* and B3LYP/6-311++G** (in Parenthesis) Optimization and the Neutron Diffraction^a Structure of Maltose.

	Exptl. ^a	Conformer I. Calcd. ^b	Δ (Exptl. – Calcd.)
Bond lengths (Å)			
C1—C2	1.535	1.536 (5)	–0.001 (0)
C1'—C2'	1.531	1.526 (7)	0.005 (0.004)
C1'—O1'	1.389	1.395	–0.006
C1—O1 (bridge)	1.414	1.422 (4)	–0.008 (–0.010)
C1—O5	1.403	1.408 (9)	–0.005 (–0.006)
C1'—O5'	1.419	1.421 (0)	–0.002 (–0.001)
C5—O5	1.434	1.446	–0.012
C5'—O5'	1.423	1.438	–0.015
C5—C6	1.516	1.524 (2)	–0.008 (–0.006)
C5'—C6'	1.518	1.526 (3)	–0.008 (–0.005)
C6—O6	1.421	1.420 (2)	0.001 (–0.001)
C6'—O6'	1.417	1.420 (2)	–0.003 (–0.005)
O1—C4' (bridge)	1.419	1.423 (5)	–0.004 (–0.006)
Nonbonded distances			
H1—H4'	2.071	2.075 (85)	–0.004 (–0.014)
O1—O4	4.41	4.50	0.11 (0.11)
O1—O1'	5.47	5.48	–0.01 (–0.01)
Bond angles (deg)			
C4—C5—C6 (ring)	112.2	114.3 (2.8)	–2.1 (–0.6)
C4'—C5'—C6' (ring)	114.2	113.6	0.6 (0.6)
C6—C5—O5 (exo)	105.7	105.1 (9)	0.6 (–0.2)
C6'—C5'—O5' (exo)	107.5	105.4 (6.0)	2.1 (1.5)
C5—O5—C1 (ring)	113.8	115.4 (8)	–1.6 (–2.0)
C5'—O5'—C1' (ring)	112.7	114.0 (1)	–1.3 (–1.4)
C1—O1—C4' (bridge)	117.8	119.1 (3)	–1.3 (–1.5)

We examined this situation in Paper III¹⁴ where the effect of water and molecular dynamics on the average solution conformation is described.

A comparison of Type I conformers, including I, IV, V, VII, VIII, and IX (Table III and Figure 2), is made in Table VI. Letters describing the conformations are provided in Table VI to help determine the orientation of groups during the discussion. Obviously, each conformer has an energy penalty associated with the variation of the ω side chains from the global minimum energy structure. One example is the rotation of the ω1H rotation from g[–] to g⁺ between conformers I and IV. This rotation resulted in a loss of energy of ~2 kcal/mol. Further, specific ω-hydroxyl group conformations may lead to close interactions between the 6- and 6'-position hydroxymethyl groups, such as that found for Conformer IV, and are of higher energy than a conformation without that specific close interaction, such as found in Conformer I (HO6—O6' =

3.5 Å). By changing the interactions between the 6-positions and also keeping the remaining sections of the molecules nearly the same, DFT/*ab initio* energy minimization resulted in several quite different backbone conformations for very similar starting structures. An example of near-energy equivalence occurs in conformers V and IX, where ω1H, ω1', ω1'H, and ω1' are nearly identical between these two conformers, while χ² differs being g⁺ in V and g[–] in IX. The result is that the HO2—O3' distance is shorter in V (1.89 Å) than in IX (1.96 Å), and yet Conformer IX is 0.9 kcal/mol lower in energy relative to Conformer V. Clearly, the orientation of the χ² hydroxyl group is partially responsible for considerable energy change when going between g[–] and g⁺. It is not clear where the entire increase in energy arises because the backbone dihedral angles have moved for these two conformations with IX being closer to the backbone conformation of Conformer I than of IV. A more severe energy loss is found upon

TABLE V.
(Continued)

	α -Ring	β -Ring	α -Ring	β -Ring	$\Delta - \alpha$	$\Delta - \beta$
Ring torsion angles, axial						
C1—C2—C3—C4	−54.7	−51.4	−55.6 (5)	−54.3 (3.8)	−0.9 (−0.8)	−2.9 (−2.4)
C2—C3—C4—C5	54.6	53.9	56.1 (5.2)	53.4 (2.4)	−1.5 (−0.6)	0.5 (1.5)
C3—C4—C5—O5	−55.5	−59.6	−55.8 (4.2)	−54.6 (3.7)	−0.3 (−1.3)	5.0 (−5.9)
C4—C5—O5—C1	59.6	64.8	59.1 (7.5)	60.6 (2)	0.5 (2.1)	4.2 (4.6)
C5—O5—C1—C2	−60.6	−61.7	−58.5 (7.9)	−62.3 (1)	2.1 (2.7)	−0.5 (−0.6)
O5—C1—C2—C3	57.4	53.9	55.2 (5)	57.2 (0)	2.2 (1.9)	−3.3 (−3.1)
O5—C5—C6—O6	59.1	−62.4	55.7 (9.0)	−63.1 (2.0)	3.4 (0.1)	−0.7 (0.4)
C1—C2—O2—H2	−48.3	75.7	−33.9 (7.2)	64.5 (3.0)	14.4 (11.1)	11.2 (12.7)
C2—C3—O3—H3	−138.8	−75.3	−47.1 (8.8)	−51.2 (2.1)	91.7 (90.0)	24.1 (23.2)
C3—C4—O4—H4	65.5	—	48.0 (50.1)	—	17.5 (15.4)	—
O5—C1—O1—C4' (ϕ)	−121.7	—	108.0 (12.3)	—	13.7 (9.4)	—
H1—C1—O1—C4' (ϕ_H)	4.8	—	−9.2 (−4.9)	—	14.0 (9.7)	—
C1—O1—C4'—C3' (ψ)	—	132.8	—	125.2 (9.8)	—	7.6 (3.0)
C1—O1—C4'—H4' (ψ_H)	—	13.3	—	5.7 (10.7)	—	7.6 (2.6)
Ring twist						
C4'—O1—C1—O4	180.0		165.7 (170.2)		14.3 (10.2)	
C1—O1—C4'—O1'	−163.0		−174.6 (−169.5)		11.6 (6.5)	
Virtual bond angle						
O4—O1 and O1—O1'	157.0		152.0 (152.1)		5.0 (4.9)	

^a Ref. 25.
^b Differences in geometry for the B3LYP/6-311++G** results are presented in parenthesis, the last value(s) that differ is shown, unless this is not clear, then the complete number is given.

going from $\omega 1 = G^+$, $\omega 1H = g^-$ in Conformer I, to $\omega 1 = G^+$, $\omega 1H = g^+$ in IV. In this case, the $\omega 1'$ and $\omega 1'H$ dihedral angles are not significantly changed, yet 2.3 kcal/mol of energy is lost despite the fact that the HO6—O6' distance becomes significantly smaller in Conformer IV (HO6—O6' = 2.0 Å) than in Conformer I.

TYPE II CONFORMERS

Conformers II and III (Type II class) differ significantly from the Type I class. In particular, the cyclic

hydroxyl groups point clockwise, with the 6- and 6'-hydroxymethyl groups also pointing clockwise. In Conformer II, the $\omega 1$ and $\omega 1H$ groups are both in the *trans* (T and t) conformation, while the $\omega 1'$ and $\omega 1'H$ are G^+ and g^- , respectively. Conformer III is only slightly lower in energy than II, even though the different orientations of the 6-positions result in different interresidue hydroxyl hydrogen bonds. It is remarkable that these two conformations (II and III), with the opposite orientation of the cyclic hydroxyl groups, are nearly the same energy as many

TABLE VI.
 ω and χ^2 Dihedral Angles and Energy Differences (B3LYP/6-31G*) for the Type I Set of Conformations.

Conformer	I	IV	V	VII	VIII	IX
$\omega 1H$	−59 (g^-)	48	−54	−55	−57	−59
$\omega 1$	55 (G^+)	61	59	59	86	57
$\omega 1'H$	59 (g^+)	50	−56	177 (t)	68	−53
$\omega 1'$	−63 (G^-)	−61	60	151 (T)	165	56
χ^2 (H2—O2—C2—C1)	−34	−41	27	−41	−41	−35
ΔE (kcal/mol)	0.0	2.3	2.7	5.4	0.2	1.8

of the Type I class of conformers, but are not as low in energy as Conformer I.

Using the DFT/*ab initio* results, one can search for reasons why Conformers II and III are higher in energy than Conformer I. Although energy differences are not easily resolved from these calculations, it is probable that the orientation of the hydroxyl groups interacting between rings may be responsible for some of the lost energy. The HO3'—O2 hydrogen bond distance in Conformer II is shorter than in Conformer I (1.85 Å in II compared to 1.97 Å in Conformer I), so one cannot attribute the loss in energy of II to the loss of interring hydrogen bonding energy. Further, this hydrogen bond is shorter in Conformer II than in III, and yet III is lower in energy than II, which is probably a compensating energy result from better interactions elsewhere in the molecule. One could argue that Conformers II and III should be lower in energy if the interring hydrogen bond is the most important source of conformational energy. To further understand this, an improper dihedral angle defining the interaction of a donor hydrogen with the lone pair electrons of an acceptor oxygen has been measured for the different conformers. In Conformer I, the improper dihedral angle defined as HO3'—C3'—O3'—H2 is found to be -140° . The other Type I structures also have this improper dihedral angle in the range of -120° to -145° . In conformers II and III, the improper dihedral angle defined by HO2—C2—O2—HO3' is found to be -177° and -179° , respectively. This value suggests that the relationship of the donor hydrogen to the acceptor oxygen is not optimal for the interring hydrogen bond in conformers II and III because the hydrogen bond lies directly in the plane of the H—O—C group, bisecting the lone-pair electron orbitals. In Conformer I and other type I conformers, the hydrogen atom is nearly optimally directed toward the lone-pair orbitals. The effect that this directional relationship of the lone-pair electrons has on the hydrogen bonding cooperativity is not clear, although one would suggest that it modifies the cooperative effect considerably.

A second parameter examined is the improper dihedral angle defined as C—O—O—C. In the methanol dimer case, this dihedral angle is found to be approx. $\pm 79^\circ$ (DFT/*ab initio* result, this work unpublished), and can be compared to values of C2—O2—O3'—C3' of -19.6° for Conformer I and -71.5° for Conformer II. In this case, the structural parameters of Conformer II are closer to those found from the methanol dimer study (this work, unpublished), indicating that Conformer II should have

a lower energy form as a result of these structural features. Because this is not the case, we are at a loss to suggest where the energy differences between Conformer I and Conformer's II and III arise. In an empirical sense, the exo-anomeric effect suggests that the O2 oxygen lone-pair orbitals are in conflict with the bridge O1 oxygen, this may be a source of the energy difference between Conformers II and I.

TYPE VI CONFORMERS

Conformers VI and X have their ψ dihedral angle flipped by $\sim 180^\circ$ relative to Conformer I types. This conformational change results in the 6-position hydroxymethyl being on the opposite side of the disaccharide relative to the 6'-position. In VI, a hydrogen bond of 2.00 Å length between HO6 and O2' stabilizes the conformation with the nonreducing ring hydroxyl groups oriented counterclockwise and the reducing ring hydroxyl groups now clockwise oriented. The HO6' is directed counterclockwise and toward the O5' atom. Both ω s are G^+ with both ω_{HS} in the g^- conformation. The energy of these conformations is high, and this is in agreement with their relative sparsity in experimental polysaccharide structures.

CONFORMER VIII

This conformation is unique, in that it allows the HO6' hydrogen to come very close (1.78 Å) to the O5 ring ether oxygen. At the same time, HO6 approaches the O6' oxygen as a hydrogen bond interaction (1.98 Å), and the HO2—O3' hydrogen bond is only 2.01 Å. The net result of these three close interactions is a conformation only 0.2 kcal/mol higher in energy than Conformer I. To our knowledge, this conformation has not been suggested previously as a possible low energy form, due to the difficulty of empirical force fields in reproducing such a conformer. We will return to this conformation again in discussions of the higher level basis set calculations at B3LYP/6-311++G**.

Comparing the two low energy maltose conformers, i.e., I and VIII, we also note that the backbone ϕ and ψ values are similar (-6.5° , 17.3° in VIII; -9.2° , 5.7° in Conformer I), indicating that one can move from one to another with only dihedral angle changes in side-chain ω -groups. It is of interest to note that the glycosidic bond angles (C1—O1—C4') are fairly large (120.1° in VIII; 119.2° in I), which might seem unusual with such different interring hydrogen bonding patterns. Bond lengths

of the two conformers reflect the hydrogen bonding differences, that is, the C1—O1 bond length is 1.422 Å in I, and shorter (1.412 Å) in VIII; C1—O5 is 1.408 Å in I and longer (1.417 Å) in VIII. The bond length differences must reflect a charge migration resulting in shortening the C1—O5 bond as the O5 oxygen electrons are drawn toward the approaching HO6' atom and subsequent shortening of the C1—O1 bond. This strong hydrogen bonding interaction is also reflected in the dihedral angles around the ring O5 oxygen, that is, the dihedral angle defined as, C4—C5—O5—C1, is 59.1° in I and 63.3° in VIII, a significant 4° difference. A check for consistency can be made using the comparable dihedral angle in the reducing sugar, and we find little difference in the dihedral angles around O5' for the two conformers. Apparently, the approach of the HO6' hydrogen either places some attractive force on the O5 oxygen lone-pair electrons, or as a result of the bond-length changes, a torsional rotation is caused around this position in the ring. The donor hydrogen, HO6', projects at an improper dihedral angle relative to the O5 oxygen of -117° , in excellent agreement with the expected direction of one of the lone pair electron orbitals ($\sim -120^\circ$). Again, the stability of this conformation is quite remarkable. The magnitude of the geometry differences is such that modeling this conformation with empirical harmonic functions is difficult, as described in Paper II.¹³

B3LYP/6-311++G** RESULTS

The B3LYP/6-31G* functions and basis set have been questioned because of possible energy differences arising from basis set superposition errors in the study of hydrogen bonding interactions in carbohydrates.^{7h} To examine the possible differences higher level basis sets may make to the calculations presented here, we have carried out studies on some of the optimized maltose conformers at the 6-311++G** level, retaining the B3LYP density functional form. Differences in selected bond lengths, bond angles, dihedral angles, and energies between geometry optimized B3LYP/6-31G* structures and those from the extended basis set, B3LYP/6-311++G**, are presented in Table III for Conformers I, II, III, IV, and VIII.

Results from geometry optimization of the five conformers using the more robust basis set showed, in general, very small deviations in geometry between the two basis sets. The cyclic hydroxyl groups rotated slightly to achieve dihedral angles $\sim 2\text{--}3^\circ$ closer to $\pm 60^\circ$. Upon increasing the cyclic dihe-

dral angles, the hydrogen bond lengths increased around the ring. However, in Conformer I the interresidue hydrogen bond length between H2 and O3' decreased (-0.01 Å), while in Conformer II the HO3'—O2 hydrogen bond increased ($+0.03$ Å) upon optimization at the larger basis set. The small change in dihedral angles of $\phi(\text{H})$ and $\psi(\text{H})$ ((I) $-9.2^\circ, 5.7^\circ \rightarrow -4.7^\circ, 10.7^\circ$; (II) $-7.4^\circ, -28.6^\circ \rightarrow -9.1^\circ, -21.0^\circ$; (III) $-17.8^\circ, -17.3^\circ \rightarrow -14.5^\circ, -16.8^\circ$; (IV) $-52.9^\circ, -35.2^\circ \rightarrow -50.5^\circ, -34.5^\circ$; (VIII) $-6.5^\circ, 17.4^\circ \rightarrow -4.4^\circ, 19.3^\circ$) found between basis sets indicates a change in interresidue interaction with change of basis set, most probably due to the added diffuse functions on oxygen atoms. Two contributions to these small changes are the interresidue hydrogen bonding between hydroxyl groups and the interaction between a hydroxyl hydrogen (HO6', for example) and an ether ring oxygen (O5). As added evidence of the action of the diffuse functions we examined the O—H bond lengths. The new O—H bond lengths are consistently shorter with the larger basis set (see Table III) than those found with the B3LYP/6-31G* set, again adding to the apparent lengthening of the cyclic hydroxyl hydrogen bonds. However, in Conformer I the O2—HO2 bond length is considerably longer than the cyclic hydroxyl O—H bonds with the extended basis set, being 0.973 Å compared to 0.979 Å for the B3LYP/6-31G* set. These distances are consistent with the shorter interresidue hydrogen bond. In Conformer II, the O3'—HO3' bond length is lengthened relative to the other cyclic hydroxyl groups, again because of the short (1.880 Å) hydrogen bond to O2. Further, the C—O—H bond angle increase of several degrees from the larger basis set is a small but significant result. There are no significant differences between basis sets in the angles around the anomeric hydrogen atom.

Another result from the 6-311++G** level calculations was the lengthening of the H—O hydrogen bond of the CH₂—OH group with the ring ether oxygen (O5). In Conformer I, the HO6—O5 distance is somewhat short, 2.292 Å at the B3LYP/6-31G* level, while it has lengthened to 2.434 Å at the optimized B3LYP/6-311++G** level. In Conformer VIII, the change in the HO6'—O5 interaction becomes more important, although the result in terms of change in the backbone ϕ and ψ values is small. In this particular interaction in Conformer VIII (see Fig. 1), multiple hydrogen bonding is localized at the ring ether oxygen (O5) from both the 6- and 6'-hydroxymethyl groups. This conformation is increased in energy relative to Conformer I (0.2 at the 6-31G* to 1.5 kcal/mol at the 6-311++G** level)

upon geometry optimization, and upon examining the extended basis set results we find an opening of the complex hydrogen bond network, with the HO6' to O5 distance longer (1.80 Å vs. 1.78 Å) and the HO6 to O6' distance longer (2.11 Å vs. 1.98 Å) than found from the B3LYP/6-31G* structure. The increase in energy difference between conformers is contrary to recent work on glucose,^{7h} where the authors found that energy differences at larger basis sets were consistently smaller than those found at the less robust basis set when considering conformational differences in the hydroxymethyl group. After geometry optimization at the larger basis set, Conformation VIII is no longer the second lowest energy conformation for the maltose series, rather Conformer II is slightly lower in energy than VIII.

The question of the correct energy differences requires more study, but for simple molecules without stress it is probably acceptable to use single energy B3LYP/6-311++G** results from geometry optimized structures at the B3LYP/6-31G* basis set.^{7h} For example, the change in energy going from the 0th energy at the B3LYP/6-31G* optimized geometry to the optimized B3LYP/6-311++G** energy is generally small, being 0.97 kcal/mol for Conformer I, 0.86 kcal/mol for Conformer II, 0.81 kcal/mol for Conformer III, 0.79 kcal/mol for Conformer IV, and 0.70 for Conformer VIII. These energy changes are small relative to the total molecular energy, and suggest that the B3LYP/6-31G* geometry is very close to that obtained using the extended basis set. This is also born out upon examination of the final geometry after optimization. However, one must be careful in the interpretation of these numbers because Conformers III and VIII increased in relative energy upon going to the B3LYP/6-311++G** level.

Finally, we wish to note the difference in optimization time for the two basis sets. Although the optimized geometry was established at the B3LYP/6-31G* level (~4 h/cycle), it required from 11 to 35 additional cycles of optimization at the B3LYP/6-311++G** level when starting from the results of the previous basis set. Each cycle at the extended level took approximately five times as long as at the B3LYP/6-31G* level.

GEOMETRY

In this section we note a number of interesting and significant changes in molecular geometry that arise from the conformational differences of the

10 B3LYP/6-31G* and five B3LYP/6-311++G** conformers found for the maltose molecule.

BOND LENGTHS

In almost all of the Type I conformations, the C1—O1 bond length is long (1.422, 1.439, 1.418, 1.423, 1.423, 1.421 Å) compared to Type II conformers (1.408 and 1.406 Å). Because the C1'—O1' bond remains the same throughout both types of conformations and the dihedral angles are not significantly different, one can suggest that this bond length difference is significant, and may be part of the energy difference described previously. The opposite trend occurs for the C1—O5 bond length where most Type I conformers have shorter C1—O5 bonds than the Type II conformers, the exceptions being conformers VII and VIII. No other bond lengths show significant patterns of differences between these two conformer types. In the case of the C5—C6 bond lengths, the higher level basis set results do not show significant shortening compared to the B3LYP/6-31G* results (see Table III). Both sets of calculated C5—C6 bond lengths are longer than the experimental values (see Table V). We have no explanation for this difference, but are convinced that it is not a result of choice of basis set as other bond lengths in the molecule fit the experimental geometry very well.

BOND ANGLES

There appear to be no major differences between conformer types' I, II, or VI in the bond angles around the anomeric carbon. Further, there are no trends associated with the C1—O5—C5 angle between the conformer types. However, an interesting difference is noted for the O1'—C1'—O5' angle, with the Type II conformers having much smaller values for this angle than the Type I conformers (~106° vs. ~109°). This observation is interesting, and it appears to be one structural feature that is a direct result of the opposite direction of the hydrogen bond network between the two conformer types. In Type II conformers, the HO1' hydroxy hydrogen points away from the ring ether oxygen, O5', thus pointing the lone-pair electrons of O1' toward O5'. This orientation not only costs energy from electron cloud overlap, it also costs energy because of a removal of the favorable HO1'—O5' hydrogen bonding interaction. In an attempt to compensate and remove the electron cloud interactions, the bond angle gets smaller in the Type II conformer.

Conclusions

The geometry of maltose is very well reproduced at the two basis sets, as described above, but there remain questions concerning the energy differences between conformations. Our goal was to find conformationally dependent geometry changes to use in the refinement of empirical force fields. That goal has been successfully accomplished with these calculations. However, one cannot generalize that the energy differences between conformations are always reduced at higher level basis sets because in this study some conformations have gone up and some down in energy relative to the lowest energy conformation. It appears that for complex molecules such as these, it is impossible to predict the direction the energy differences will take upon examination at higher basis sets.

The different conformations with their complex patterns of hydrogen bonding and backbone conformations have already been very useful as guides for the refinement of an empirical carbohydrate force field.^{12–14} Ongoing DFT/*ab initio* calculations²⁵ on cellobiose, a model for $\beta(1 \rightarrow 4)$ bridges in carbohydrates, are providing added molecular parameters and energies for this second anomeric type.

Acknowledgment

Names are necessary to report factually on available data; however, the USDA neither guarantees nor warrants the standard of the product, and the use of the name by USDA implies no approval of the product to the exclusion of others that may also be suitable.

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